BMJ Best Practice

Gender dysphoria in adults

Straight to the point of care

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Summary

Subspecialty consultation is required for any patient with suspected or confirmed gender dysphoria. Treatment is complex and should only be undertaken as part of a package of care provided by a multidisciplinary team with extensive experience in this area.

In children and adolescents, disorders of gender identity are particularly complicated, may have higher comorbidity, and may change form as patients mature, making specialist assessment particularly important. This topic covers the management of gender dysphoria in adults only.

Gender dysphoria is not commonly pronounced enough to prompt patients to seek medical intervention. Dual role transvestism is the most common manifestation.

Most clinics treat patients with hormones only when they are adults and have already changed their social gender role (or, occasionally, have a definite and agreed time when they will do so).

Most clinics will not undertake bilateral mastectomy unless there has been a change of social gender role from female to another, demonstrably stable, social gender role, usually male.

No clinic will undertake genital surgery unless there has been agreement from 2 appropriately trained professionals and the patient has been living with demonstrated success in their new gender role for at least 1 year.

Definition

Gender nonconformity is when a person's gender identity, role, or expression differs from the cultural norms prescribed for people of a particular gender.[1]

Gender dysphoria is present when there is a distressing dissonance between a person's biological sex and associated social gender role, as assigned at birth, and that person's sense of their own gender.[1]

Only some gender nonconforming people experience gender dysphoria at some point in their lives.[1]

The term "gender identity disorder" has been replaced by "gender dysphoria" in the latest "Diagnostic and statistical manual of mental disorders, 5th edition" (DSM-5) after consideration by the American Psychiatric Association.[2] [3]

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Epidemiology

Around 7 to 9 people in every 100,000 have gender dysphoria pronounced enough to seek medical attention.[12]

In the US, there seems to be no significant association with social class, intelligence, or ancestry. Presentations to gender identity clinics are becoming more common, but this may reflect better awareness of, and access to, treatment, rather than increasing incidence.[1]

The most common manifestation of gender dysphoria in born males is dual role transvestism (also known as cross-dressing; the term "transvestite" is sometimes considered pejorative, although is used within this topic given that dual role transvestism is an "International classification of Diseases, version 10" diagnosis). Dual role transvestism can be described as the wearing of clothes of the opposite sex for part of the time in order to enjoy the temporary experience of membership of the opposite sex, but without desire for something more permanent. No sexual excitement accompanies the cross-dressing, which distinguishes it from fetishistic transvestism. Dual role transvestism is not often brought to the attention of doctors.

More pronounced gender dysphoria is characterized by the desire to live and be accepted in a social gender role other than that assigned at birth, and is usually accompanied by a sense of discomfort with one's own body, particularly those primary and secondary sexual characteristics others use to assign social gender role, such as genitals, breasts, or facial hair. The desire has usually been present for at least 2 years, and must not be a symptom of a mental disorder, although it can coexist with such a disorder;[4] discerning that both are independently present requires skilled gender identity specialists with a background in psychiatry or psychology. Gender dysphoria may be associated with intersex, genetic, or sex chromosome abnormalities. These should not be assumed to be causative, and their presence rarely alters clinical management. The adjective "transsexual" is often applied by the medical profession to describe people who seek to change or who have changed their primary and/or secondary sex characteristics through feminizing or masculinizing medical interventions (hormones and/or surgery), typically accompanied by a permanent change in gender role.[1]

Etiology

It is not clear what causes gender dysphoria. At first, hypotheses about causation addressed psychological factors and came mostly from a psychoanalytic perspective.[8] Over the decades, though, available evidence has suggested a multifactorial etiology, with biological factors rising in importance.[13]

There is known to be an elevated rate of gender dysphoria among people with Klinefelter syndrome.[14] It is also known that born males with disorders of gender identity are more likely than the general population to be left-handed.[15] Family trees of born-male patients show a relative lack of maternal uncles, and these patients are more likely to be lower-down in male birth order.[16] One hypothesis arising from these findings supposes that in these families, women mount an immune response to a Y chromosome in pregnancy, the titer rising with each successive male pregnancy.

Some observations suggest children and adults with disorders of gender identity show more features of autism spectrum disorder (ASD) than the general population.[17] [18] At one gender clinic prevalence of autistic traits consistent with a clinical diagnosis of ASD among individuals undertaking treatment was 5.5%, compared with reports of 0.5% to 2.0% ASD diagnoses in the general population.[19] People with concurrent gender dysphoria and ASD sometimes have an atypical presentation of gender dysphoria, which makes a correct diagnosis and determination of treatment options for gender dysphoria more difficult.[17] [20]

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Pathophysiology

As a general rule, neurologic and physiologic function in people with disorders of gender identity appear to be the same as in the general population.

However, there does seem to be an increased rate of non-right-handedness[15] and an increased rate of both autism spectrum disorder (ASD) and features of ASD.[17] [18] [19] One small study showed that the size of the bed nucleus of the brain's stria terminalis was in keeping with the patients' sense of gender rather than their biological sex.[21] Another study showed white matter changes in born-female transsexuals prior to hormone treatment that were akin to those seen in males.[22]

Gender dysphoria is slightly more common among people with Klinefelter syndrome, partial androgen insensitivity syndromes,[23] and congenital adrenal hyperplasia.[24] [25] [26] In these circumstances, a diagnosis of gender dysphoria (not otherwise specified) applies, rather than one of transsexualism, because the latter diagnosis requires absence of any endocrine or chromosomal abnormality. This distinction is to be lost in the International Statistical Classification of Diseases and Health Related Problems (ICD)-11 and management is still as for transsexualism.

Classification

International statistical classification of diseases and health related problems (ICD-10)[4]

Dual role transvestism (also known as cross-dressing; the term "transvestite" may be considered pejorative in some parts of the world).[5]

- The wearing of clothes of the opposite sex for part of the time in order to enjoy the temporary experience of membership of the opposite sex, but without desire for something more permanent. No sexual excitement accompanies the cross-dressing, which distinguishes it from fetishistic transvestism.

Transsexualism

- The desire to live and be accepted as a member of the opposite sex, usually accompanied by a sense of discomfort with one's anatomic sex. The desire should have been present for at least 2 years, and must not be a symptom of another mental disorder or associated with any intersex, genetic, or sex chromosome abnormality.

Gender dysphoria of childhood

- A persistent and intense distress about assigned sex, together with a desire to be of the other sex. Diagnosis requires a profound disturbance of normal sense of maleness or femaleness. Diagnosis should not be made when the individual has reached puberty.

It has been established that ICD-11 will not feature gender dysphoria in the section devoted to disorders of psychological functioning, the likely destination being a section devoted to conditions related to sexual health. [WHO: International Classification of Diseases 11th Revision] (https://icd.who.int/en)

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Case history

Case history #1

A 45-year-old man, dressed as a woman, requests a prescription for estrogens and a rapid referral for gender reassignment surgery on the grounds of self-diagnosed transsexualism. They give a history of lifelong cross-dressing, which became sexually exciting at puberty. The sexual excitement diminished in his 20s, to be replaced by a sense of relaxation and comfort when in a female role, described as being able to express his feminine side. They are married, but separated, and have 2 children. The sexual content of their marriage (never very great) diminished after their birth. They hid their cross-dressing from their wife until she discovered their female clothes and assumed that they were having an affair. Although initially tolerant of their cross-dressing, she became increasingly dissatisfied as they spent more time in a female role and suggested that they might live together as sisters. Moving away from their wife and children, they began to purchase estrogens from the internet. They lived as a woman for all purposes aside from their work, where nothing was known of his female life outside. They began to feel increasingly unhappy in their male work life, feeling that they were only truly themself when living as a woman.

Case history #2

A 35-year-old woman requests treatment with androgens and a bilateral mastectomy. They look masculine and is often taken to be a male somewhat younger than their chronological age. They give a history of childhood tomboyism, and at high school was widely assumed to be lesbian. Declaring themself to be a lesbian in their late teens, they moved in lesbian social circles for some years and made relationships with women with some ease. These tended to founder after a few months because partners complained that, rather than being a masculine woman, they were more like a man. Although their libido was good and they were an attentive sexual partner, they could not bear attention being paid to their own female sexual characteristics, and the one-sided nature of the sexual relationship became, after a time, disturbing to their partners. Eventually they felt that their sense of masculinity could no longer be denied to themself and others, and decided to live as a man. They are desperate to halt their menstrual periods, seeking treatment with androgens to increase facial and body hair, and to lose their breasts.

Other presentations

The majority of born-male patients with gender dysphoria present with a background of initially fetishistic and subsequently dual role transvestism (cross-dressing). A smaller number give a history of earlier very feminine homosexuality associated with a low libido and an ever-increasing sense of femaleness that drives them to live as a woman and to be viewed by others (including gay men) as a woman. Born-female patients almost all have a history of childhood masculine behavior, and many have (for a while at least) been identified by themselves or others as masculine lesbian women. A small proportion of people of either biological sex present with pronounced gender dysphoria and cross-sex behavior in childhood, even from their earliest years. They were often taken to be the opposite sex in childhood and very often experience sexual attraction to their own biological sex. However it is important to note that childhood gender dysphoria does not necessarily continue into adulthood.[1] A number of studies in both boys and girls with gender dysphoria suggest that persistence into adulthood occurs in 6% to 27% of children.[6] [7] [8] [9] [10] [11]

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Approach

The clinician should confirm that the gender dysphoria has been present for more than 2 years, and that it is not a direct symptom of any mental illness.[4] It should also be determined whether there is a preceding history of gender dysphoria of childhood, using informants if possible.

Clinical presentation

The history should elicit whether the gender dysphoria has been preceded by fetishistic transvestism, dual role transvestism (cross-dressing), or feminine/masculine homosexuality. Unprescribed hormone and other drug consumption should be investigated, as should any earlier attempts at treatment, including surgery.

Sexual orientation is an attribute wholly distinct from gender identity, but in purely statistical terms, most born-female patients are sexually interested in women, while born-male patients might be interested in either sex and are more likely to experience a broadening or changing sexual orientation after a change of social gender role. Libido tends to be low in born-male patients and normal in born females.

Physical examination is usually normal. Clothing and hairstyle may be gender neutral or resemble those of the other sex. Vocal style and mannerisms often resemble those of the other sex, particularly in born-female patients.

It should be assessed whether there is a serious intention to change social gender role, or whether the stated desire for hormone treatment or surgery is aimed at removing the characteristics of one sex without seeking the characteristics of the other, or acquiring the characteristics of both, and vitally, with no change of social gender role at all. This last aspect is more in keeping with body dysmorphic disorder or autogynephilia.[20]

Laboratory investigations

Serum androgens should be checked. The presence of elevated serum testosterone and dihydrotestosterone and unsuppressed follicle-stimulating hormone and luteinizing hormone suggests a partial androgen insensitivity syndrome, which requires genetic counseling for the family. Low testosterone and elevated gonadotropins in males suggests Klinefelter syndrome. Elevated androgens in females may suggest polycystic ovary syndrome.

Patients being considered for hormone treatment should first be screened for contraindications.[5] Recommended blood tests include liver function tests, lipids, hematocrit and hemoglobin (to evaluate for polycythemia), and prolactin. Those receiving endocrine treatment who have relative contraindications to hormones (e.g., smoking, diabetes, liver disease, etc.) should have an in-depth discussion with their physician concerning the risks and benefits of therapy.[27] Clinicians should stress the importance of smoking cessation, as smoking increases the thromboembolic risk from estrogen treatment and polycythemia with testosterone treatment.

History and exam

Key diagnostic factors

gender dysphoria (common)

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- There should be the presence of both a desire to live as another gender and a seeking of bodily transformation to resemble as closely as possible that other gender role. This should have been present for at least 2 years. There should be absence of any psychiatric symptomatology that might directly account for these feelings.[4]

altered appearance or affect (common)

- Patients often have already taken steps regarding clothing and hairstyle in order to resemble another sex. Their mannerisms often resemble those of the other sex, particularly in born-female patients.

Other diagnostic factors

diminished sexual function or homosexuality (common)

- Libido tends to be low in born-male patients and normal in born females. Most born-female patients are sexually interested in women. Born-male patients might be interested in either sex. Sexual orientation is much less diagnostically significant than libido.

atypical speech and vocal quality (uncommon)

- Vocal quality and style of speech may resemble that of the other sex.

Risk factors

Weak

congenital adrenal hyperplasia

- Associated with a slightly elevated rate of gender dysphoria.[24] [26] [25]

partial androgen insensitivity syndromes

- Associated with a slightly elevated rate of gender dysphoria.[23]

Klinefelter syndrome

- Associated with a slightly elevated rate of gender dysphoria.[14]

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Investigations

1st test to order

Test	Result
serum testosterone • Used to exclude associated conditions. • High testosterone with high or normal follicle-stimulating hormone (FSH) and luteinizing hormone (LH) suggests partial androgen insensitivity syndrome. • Low testosterone and elevated gonadotropins in males suggests Klinefelter syndrome. • High androgens in females may suggest polycystic ovary syndrome. • Morning draw of the specimen is recommended.	**normal**
serum dihydrotestosterone • Used to exclude associated conditions. • High testosterone and dihydrotestosterone with high or normal FSH and LH suggests partial androgen insensitivity syndrome. • Morning draw of the specimen is recommended.	**normal**
serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) • Used to exclude associated conditions. • High testosterone with high or normal FSH and LH suggests partial androgen insensitivity syndrome. • Low testosterone and elevated gonadotropins in males suggest Klinefelter syndrome.	**normal**
serum prolactin • Used to exclude associated conditions. • Elevation may suggest prolactinoma or drug use. • Post-treatment, prolactin should not rise above 1000 IU. • Should be repeated every 6 months while the patient is on hormonal therapy.	**normal**
serum liver function tests • Serum aspartate aminotransferase, alkaline phosphatase, and gamma glutamyl transpeptidase should be followed up every 6 months while the patient is on hormonal therapy.	**normal baseline**
serum lipid screen • LDL-cholesterol may rarely rise with hormone treatment. Dyslipidemia should be treated as it would be for any other cause. • Should be repeated every 6 months.	**should be normal initially**
CBC • Elevated mean corpuscular volume (MCV) denotes possible alcohol use disorder. Hemoglobin (Hb) may rise following androgen treatment, particularly in smokers. • Should be followed up every 6 months.	**MCV and Hb should be normal initially**

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Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Autogynephilia	• Male patient seeks hormone treatment and/or surgery to obtain female bodily characteristics (usually breasts) but either does not want to change social gender role or makes no more than token gestures in this regard. • Often a greater degree of earlier sexual activity than in transsexualism, and a sexualized element to the desire for female characteristics (which may not be admitted).	• No distinguishing tests: diagnosis is clinical.
Body dysmorphic disorder	• Patient abhors and seeks the removal of either primary or secondary sexual characteristics but has no sense of wanting any other gender role or plan to change social gender role. • Aside from this preoccupation, function in birth gender role has often been quite good.	• No distinguishing tests: diagnosis is clinical.
Ego-dystonic sexual orientation	• Patient's main motivation is an intimate relationship with someone of the same birth sex. • Patient has very negative views about homosexuality and seeks medical explanation and legitimization of this desire.	• No distinguishing tests: diagnosis is clinical.
Psychosis	• Patient's presentation has the psychological texture of a delusion. Patient is not very worried about how others perceive him/her as a member of the opposite sex. • Often a history of psychosis or delusions. Sometimes negative symptoms or affective symptoms present at the time of interview.	• No distinguishing tests: diagnosis is clinical.

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Condition	Differentiating signs / symptoms	Differentiating tests
Fetishistic transvestism	• Wearing of the clothes of the opposite sex is associated with sexual arousal. The clothes are often sexualized. The behavior may be accompanied by masturbation. After orgasm there is often a sense of shame and the rapid removal of the clothes, accompanied by a (transitory) resolution never to cross-dress again. • Found almost exclusively in males.	• No distinguishing tests: diagnosis is clinical.
Borderline personality disorder	• Sense of identity is generally unclear, not isolated to gender identity. Beliefs about a variety of aspects of identity are intense but shallow and sometimes brief. • Other aspects of personal history are consistent with personality disorder, and this diagnosis may have already been made. Gender dysphoria is of recent onset but very intensely presented. • Borderline personality disorder should not preclude referral to a gender identity clinic but might make management more complicated.	• No distinguishing tests: diagnosis is clinical.

Criteria

International statistical classification of diseases and health related problems (ICD-10)[4]

Dual role transvestism

- Diagnosed in the context of the wearing of clothes of the opposite sex for part of the time in order to enjoy the temporary experience of membership of the opposite sex, but without desire for something more permanent.
- No sexual excitement accompanies the cross-dressing, which distinguishes the disorder from fetishistic transvestism.

Transsexualism

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- Described as the desire to live and be accepted as a member of the opposite sex. It is usually accompanied by a sense of discomfort with one's anatomic sex.
- The desire should have been present for at least 2 years, and must not be a symptom of another mental disorder or be associated with any intersex, genetic, or sex chromosome abnormality.

Gender dysphoria of childhood

- Persistent and intense distress about assigned sex together with a desire to be of the other sex. Diagnosis requires a profound disturbance of the normal sense of maleness or femaleness.
- Diagnosis should not be made when the individual has reached puberty.

Diagnostic and statistical manual of mental disorders, 5th edition (DSM-5)[2]

Gender dysphoria in adolescents and adults

- A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least two of the following:
    - A marked incongruence between one's gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics).
    - A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics).
    - A strong desire for the primary and/or secondary sex characteristics of the other gender.
    - A strong desire to be of the other gender (or some alternative gender different from one's assigned gender).
    - A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).
    - A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).
- The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- Two specifiers exist:
    - With a disorder of sex development (e.g., congenital adrenal hyperplasia).
    - Post-transition: the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least 1 cross-sex medical procedure or treatment regimen (e.g., regular cross-sex hormone treatment or gender reassignment surgery confirming the desired gender).
- Separate criteria now also exist for the diagnosis of children; however, children with gender dysphoria are not covered by this monograph. Gender dysphoria no longer comes under the category of sexual dysfunctions and paraphilic disorders and is considered a disorder in its own right. The term "gender identity disorder" has been replaced by "gender dysphoria" to avoid stigmatization. [APA: gender dysphoria] (https://www.psychiatry.org/File%20Library/Psychiatrists/Practice/DSM/APA_DSM-5-Gender-Dysphoria.pdf)

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Screening

There are currently no measures to screen the general population for disorders of gender identity. Nor does such screening seem appropriate to healthcare providers or patient groups.

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Approach

The aim of treatment is to improve the quality of life to the maximum attainable degree by means of safe and sustainable relief of gender dysphoria. An overarching principle is that reversible steps should have been successfully negotiated before irreversible steps are contemplated.[1] Further, significant or irreversible steps should be approved by two suitably qualified and experienced gender identity specialists (often, but not necessarily, mental health professionals) before they are undertaken. Subspecialty consultation is required. No medical treatment should ever be undertaken without appropriately qualified psychological support.[1]

When caring for people with gender dysphoria use their patient-identified name and gender-neutral terminology until pronoun preferences are made clear. Healthcare workers should also be aware of the lack of standardization in recording gender identity and there may be insufficient options in electronic health record platforms. When treating people who take gender-affirming hormones, it is important to remember these may affect laboratory test results (e.g., liver function tests) and modify disease-specific risk factors or increase the risk of in-hospital complications (e.g., venous thromboembolism).[28]

Quality of diagnosis

As the diagnosis is the gateway to potentially drastic and irreversible treatment, it is appropriate for comorbidities to be identified, differential diagnoses excluded, and a proper diagnosis to be made by a suitably qualified gender dysphoria specialist working in the context of a multidisciplinary team in a gender identity clinic.

Patients should have been biochemically screened for other possible diagnoses, such as Klinefelter syndrome, polycystic ovary syndrome, congenital adrenal hyperplasia, or a partial androgen insensitivity syndrome. Such screening ensures that the patient is fit to be treated with cross-sex hormone treatment, when this is indicated; a partial androgen insensitivity syndrome also indicates a need for genetic counseling for the patient's family.

Practical, real world experience

The process of fully adopting a new or evolving gender role or gender presentation in everyday life is known as the ‘real world’ or ‘real life’ experience. Many clinicians maintain that hormone treatment should generally not be started unless the patient has already changed gender role.[27] This includes legally changing registration to that of the preferred sex and changing name on all documents. All other people should be made aware of this change and asked to treat the patient as the chosen sex, even if they know that this was not always the case. The degree to which the change in gender expression and role can be practically applied then becomes apparent to clinician and patient alike. Changes of social gender role to a real life, nonbinary role may be harder to accomplish than patients anticipate, and after practical experience, can be modified into a more direct change to another, more distinct, social gender role.[27]

Some patient groups maintain that hormone treatment should precede a change of gender role. However, this approach involves a prolonged period of potentially dangerous treatment with hormones that may result in the patient being forever unhappy with the degree of bodily change and indefinitely postponing any change of role.

Patients with autogynephilia seek hormone treatment without any change of gender role and may put forward this argument (explicitly or covertly) to achieve that aim. Their autogynephilia may subsequently dissipate, leaving them with unwanted feminization.

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There is universal agreement that a period of practical experience of at least 1 year (including at least 1 year of consistent hormone treatment, unless unsuitable or contraindicated) should precede any genital surgery.[1] [27] Longer periods would be needed if there are any problems living in the new gender role, to allow time for these problems to be addressed. Patients should not undergo surgical treatment until they are thriving (not merely surviving) in their new gender role.

Cross-sex hormone treatment

Hormone therapy involves giving exogenous hormones in order to:[1] [27]

- Reduce endogenous hormone levels (with a resultant reduction in secondary sex characteristics of the person's biological sex)
- Replace these endogenous hormones with those of the reassigned sex following principles of hormone replacement for hypogonadal patients.

Individualized treatment is required based on the patient's goals, any medical contraindications, and the side effect profile of the medications used. Hormone therapy may lead to irreversible physical changes, and so informed consent is essential, including a full discussion of the risks and benefits, and effects on reproductive capacity.[1] Screening for and addressing acute and chronic mental health concerns is a key part of this process.[20]

Hormone treatment varies with the birth sex of the patient. Most practitioners take the view that hormone treatment should come after a change of gender role.[27] Rarely, hormone treatment is used for patients who do not wish to make a social gender role transition or undergo surgery, or who are unable to do so.[1]

Transgender care is an interdisciplinary field, and so coordination of care and referral for hormone treatment within a patient's overall care team is recommended. The World Professional Association for Transgender Health guidelines advise that health professionals who recommend hormone therapy share the ethical and legal responsibility for that decision with the physician who provides the service.[1]

Criteria for hormone therapy include the following:[1]

- Persistent, well-documented gender dysphoria
- Capacity to make a fully informed decision and to consent for treatment
- Relevant medical or mental health problems are well controlled.

Hormone treatment in born males

- Estrogen, with or without gonadotropin suppression with a gonadotropin-releasing hormone (GnRH) agonist, is used in born males. However, there are no randomized controlled trials to assess the safety and efficacy of this treatment.[29] While androgen blockers such as spironolactone, cyproterone, and 5-alpha reductase inhibitors are noted by some guidelines to be the most frequently used gonadotropin suppression agents,[1] the author of this topic does not recommend them because their frequent use is reflective not of superiority but rather of local or national formulary availability or economic affordability. The ideal agent is one that inhibits all testicular function with minimal or zero side effects, something which can be achieved with a GnRH agonist. Disadvantages of GnRH agonists are the requirement for parenteral administration and a relatively greater cost, which sometimes prevents placement on available formularies.
- Risks associated with estrogen therapy in born males include:[27]
    - Very high risk of adverse outcomes

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        - Thromboembolic disease
    - Moderate risk of adverse outcomes
        - Macroprolactinoma
        - Breast cancer
        - Coronary artery disease
        - Cerebrovascular disease
        - Cholelithiasis
        - Hypertriglyceridemia.
- Contraindications to feminizing treatment with estrogen include:[1]
    - Previous venous thrombotic events related to an underlying hypercoagulable state
    - History of estrogen-sensitive cancer
    - End-stage chronic liver disease.

Hormone treatment in born females

- Gonadotropin suppression is not usually needed in born females, as androgens alone suppress ovarian function very well.
- Risks associated with testosterone therapy in born females include:[27]
    - Very high risk of adverse outcomes
        - Polycythemia (hematocrit > 50%)
    - Moderate risk of adverse outcomes
        - Severe liver dysfunction (transaminases > threefold upper limit of normal)
        - Coronary artery disease
        - Cerebrovascular disease
        - Hypertension
        - Breast or uterine cancer.
- Contraindications to masculinizing treatment with testosterone include:[1]
    - Pregnancy
    - Unstable coronary artery disease
    - Untreated polycythemia with a hematocrit of 55% or higher.

All patients should be offered the opportunity for gamete storage before hormone treatment, as is the case for any medically mandated treatment that removes natural fertility.[1]

It typically takes 2 or more years for patients to achieve maximal masculinizing/feminizing results from hormones. If there was gonadal suppression with a GnRH agonist, the same dose will be needed after any genital surgery; although, in later life doses might need to be lowered to achieve the same hormone levels, as hepatic sex steroid metabolism can decrease with age.

For patients who go on to have gonadectomy, hormone therapy with estrogen or testosterone is usually continued lifelong, unless contraindications develop.[1]

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Criteria for genital surgery and removal of gonads

Some patients with gender dysphoria are able to live successfully in their preferred gender role without surgery, but for others, genital surgery is the final (and most considered) step in the treatment process.[1] As with hormone treatment, the mental health professional who recommends genital surgery shares the ethical and legal responsibility for that decision with the clinician who performs the surgery. The criteria for starting genital surgery are the same as for starting hormone therapy, with one additional criterion (due to its increased invasiveness):[1]

- One year of continuous hormone therapy and living in the desired gender role (unless hormone therapy is not medically indicated).

Endocrine Society clinical practice guidelines recommend that genital surgery and removal of gonads should be considered only if the physician overseeing hormone treatment and the mental health professional overseeing the patient's gender dysphoria both agree that surgery is medically necessary and beneficial for the patient overall, and the clinician overseeing hormone treatment has medically cleared the patient for surgery.[27]

Born males: adjunctive surgeries and treatment

Hair removal

- This can be done with electrolysis or laser treatment.[1] All other methods are non-permanent. Laser treatment works only with dark-colored hair and light-colored skin.

Head and neck surgery

- Thyroid cartilage reduction surgery is sometimes needed in tall, thin, born-male patients whose thyroid cartilage is unacceptably prominent. It is usually an unproblematic procedure. It can be combined with a cricothyroid approximation.
- Cricothyroid approximation can be done alone or combined with a thyroid cartilage reduction. It alters vocal quality to a more feminine pitch. It should only be attempted when speech therapy has failed, and usually requires follow-up speech therapy.
- Craniofacial surgery is a complex and sometimes very radical surgery that is sometimes helpful but should only be contemplated when treatment with hormones has been fully utilized and when simpler cosmesis has failed.

Augmentation mammoplasty

- Although not a formal prerequisite, it is recommended that patients receive feminizing hormone treatment (for a minimum of 12 months) prior to surgery.[1] In the author's experience, a minimum of 2 years is preferable. This is because it can be aesthetically problematic if natural breast development under estrogen stimulation follows an augmentation mammoplasty.[27]

Genital surgery

- This procedure is indicated only when the patient has experienced a minimum of 1 year of continuous hormone therapy and living in the desired gender role (unless hormone therapy is not medically indicated).[1] Many clinics would want 2 years.The patient must over that period of time have shown improved psychological, social, and, probably, occupational function.

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- The surgery uses the existing genitals to fashion a vulva, neoclitoris and hood, labia, and (often) neovagina. Preoperative genital hair removal is sometimes needed, particularly in patients who have been circumcised. The cosmetic results can be very good.

Born females: adjunctive surgeries and treatment

Bilateral mastectomy

- There is no consensus about when born-female patients should undergo bilateral mastectomy.[27] Although hormone therapy is not a formal prerequisite to bilateral mastectomy,[1] nearly all practitioners take the view that bilateral mastectomy should come after a change of gender role and treatment with androgens. Some patient groups argue that it should precede both. Body weight and shape can change considerably when patients are treated with androgens, and it may be that an initially good postsurgical appearance alters negatively with subsequent androgen treatment. Difficulties may arise when a patient initially asserts that a non-binary role is desired and requests bilateral mastectomy and chest reconstruction without preceding treatment with testosterone. There may then be a subsequent evolution to a more clearly male role and corresponding need for testosterone treatment, which may have a negative impact on the patient's postsurgical appearance.

Hysterectomy and bilateral oophorectomy

- Consideration of hysterectomy and bilateral oophorectomy is recommended within 2 years of the start of androgen treatment to obviate the risk of gynecologic malignancy.[27]
- For patients who have not had previous abdominal surgery, the laparoscopic technique for hysterectomy and bilateral oophorectomy is recommended to avoid a lower abdominal scar.[1]
- Other approaches are transvaginal and transabdominal. Vaginal access may be difficult as most patients are nulliparous and have often not experienced penetrative intercourse.[1] A transabdominal approach may utilize any incision other than a Pfannenstiel incision, as this incision is pathognomonic of gynecologic surgery and the resulting scar looks odd in a male.

Phalloplasty

- This complex, often multistage procedure is indicated only when the patient has lived in a male role receiving continuous hormone treatment, unless contraindicated, for 1 year at the very minimum[1] (many clinics would want 2 years). The patient must over that period of time have shown improved psychological, social, and, probably, occupational function.
- Donor sites for phalloplasty can include the forearm, abdominal skin, or tissue from elsewhere on the body. The complexity, duration, and expense of the procedure are such that only a minority of patients choose to undergo this surgery. The cosmetic and functional results are fairly good, but the result in even the best centers is clearly distinguishable from a native penis.

Craniofacial surgery

- This complex and sometimes very radical surgery is sometimes helpful but should only be contemplated when treatment with hormones has been fully utilized and when simpler cosmesis has failed.[27]

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Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Ongoing (summary)		
born males		
successful role change for ≥1 year	1st	observation in changed sex role for ≥1 year
	plus	estrogens
	adjunct	androgen suppression therapy
	adjunct	hair removal
	adjunct	head and neck surgery
	adjunct	augmentation mammoplasty
	adjunct	genital surgery
born females		
successful role change for ≥1 year	1st	observation in changed sex role for ≥1 year
	plus	androgens
	adjunct	bilateral mastectomy
	adjunct	hysterectomy and bilateral oophorectomy
	adjunct	phalloplasty
	adjunct	craniofacial surgery

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Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

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Ongoing

born males

born males — **1st** — **observation in changed sex role for ≥1 year**

» Treatment for gender dysphoria should not typically be started unless the patient has already changed gender role. This means legally changing registration to that of the preferred sex and changing the name on all documents. All other people should be made aware of this change and asked to treat the patient as this sex, even if they know this was not always the case.

» There is universal agreement within international standards of care that practical experience of at least 1 year (plus 1 year of continuous hormone treatment) should precede any genital surgery.[1] [27] Longer periods would be needed if there are any problems living in the new gender role. Patients should not undergo surgical treatment until they are thriving (not merely surviving) in their new gender role.

» Some patient groups maintain that hormone treatment should precede a change of gender role, but this approach involves a prolonged period of potentially dangerous treatment with hormones and may result in the patient being forever unhappy with the degree of bodily change and indefinitely postponing any change of role.

» Patients with autogynephilia seek hormone treatment without a change of gender role and may put forward this argument (explicitly or covertly) to achieve that aim. Their autogynephilia may subsequently dissipate, leaving them with unwanted feminization.

successful role change for ≥1 year — **plus** — **estrogens**

Treatment recommended for ALL patients in selected patient group

Primary options

» estradiol valerate: 2 mg orally once-daily for at least 3 months; then 2 mg twice-daily for at least 3 months; then 2 mg three times-daily for at least 3 months; then increase by 2 mg/day increments every 3 months, according to response if feminization is insufficient after 9 months of treatment, particularly in large patients

OR

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Ongoing

» estradiol transdermal: consult specialist for guidance on dose; multiple patches may need to be used to achieve a suitable dose

» Criteria for hormone therapy include the following:[1] persistent, well-documented gender dysphoria; capacity to make a fully informed decision and to consent for treatment; relevant medical or mental health problems are well controlled.

» Contraindications to feminizing treatment with estrogen include:[1] previous venous thrombotic events related to an underlying hypercoagulable state; history of estrogen-sensitive cancer; end-stage chronic liver disease.

» Most clinics require the patient to have already started living in the new gender role before this treatment is considered.

» Treatment is preferably done working as part of a multidisciplinary team containing (or having easy access to) an endocrinologist.

» Cross-sex hormone treatment aims to elicit in a born-male patient the secondary sexual changes seen in born females at puberty. These changes will be superimposed on whatever male pubertal changes have already occurred and will not reverse them.

» Progesterone is not indicated, as it has no feminizing effects and is found in born-female puberty only after all breast growth has been completed. Progesterone raises the risk of breast cancer and has been associated with depression.[1]

» Estrogen treatment is associated with a dramatic drop in erectile capacity and libido (both usually welcomed by the patient). There is no effect on vocal quality. Facial and bodily hair growth is slowed only slightly and never stopped.

» The most serious side effect is thromboembolic disease risk (the risk is raised about 20 times from controls). For this reason, non-smoking status is required. Normal liver function tests (LFTs), lipid profile, and prolactin should be confirmed before starting treatment.[27] After 3 months, the first two should remain normal and the prolactin <1000 IU.[30] Rarer side effects are abnormal LFTs or dyslipidemia with insulin resistance.

» The most common side effect is increased appetite, which can lead to obesity. There is

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Ongoing

sometimes a modest redistribution of fat into a more feminine pattern.

» Treatment should start with moderate doses and build over time to a dose that produces a serum estradiol in the normal female premenopausal range. High-dose treatment from the outset is associated with early duct fusion and the eventual formation of small, hard, conical breasts that cannot be made larger or more naturally textured with any subsequent hormonal manipulation.

» After dose escalation to three times daily, estradiol level should be confirmed to lie in the normal female pre-menopausal range.

» It typically takes 2 or more years for patients to achieve maximal feminizing results from hormones. If there was gonadal suppression with a gonadotropin-releasing hormone agonist, the same dose will be needed after any genital surgery, although in later life doses might need to be lowered to achieve the same hormone levels as hepatic sex steroid metabolism can decrease with age.

» For patients who go on to have orchidectomy, hormone therapy with estrogen is usually continued lifelong, unless contraindications develop.[1]

adjunct **androgen suppression therapy**

Treatment recommended for SOME patients in selected patient group

Primary options

» goserelin: 10.8 mg subcutaneously every 3 months

» Used in those born-male patients in whom native androgen production is not suppressed by full-dose estrogen therapy.[30] These tend to be younger patients (<40 years).

» In these cases, adjunctive treatment with a gonadotropin-releasing hormone (GnRH) agonist (used exactly as for prostate cancer) is indicated. This treatment carries fewer side effects than when used for prostate cancer and is usually well tolerated, with bone density being protected by the parallel sex steroid therapy.

» Additional antiandrogens in the form of androgen receptor blockers are not recommended because they can cause depression, lethargy, and fatigue, and can be hepatotoxic. They are sometimes used at the

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Ongoing

start of treatment with gonadotropin-releasing hormone agonists to prevent the effects of the initial androgen surge that this treatment causes.

» While androgen blockers (such as spironolactone, cyproterone, and 5-alpha reductase inhibitor) are noted by some guidelines to be the most frequently used androgen suppression agents,[1] the author of this topic does not recommend them because their frequent use is reflective not of superiority but rather of local or national formulary availability or economic affordability. The ideal agent is that which inhibits all testicular function with minimal or zero side effects, something which can be achieved with a GnRH agonist. Disadvantages of GnRH agonists are the requirement for parenteral administration and a relatively greater cost, which sometimes prevents placement on available formularies.

adjunct **hair removal**

Treatment recommended for SOME patients in selected patient group

» This can be done with electrolysis or laser treatment. All other methods are non-permanent. Laser treatment works only with dark-colored hair and light-colored skin.

adjunct **head and neck surgery**

Treatment recommended for SOME patients in selected patient group

» Thyroid cartilage reduction is a usually unproblematic procedure that is sometimes needed in tall, thin, born-male patients whose thyroid cartilage is unacceptably prominent. It can be combined with a cricothyroid approximation.

» A cricothyroid approximation procedure can be done alone or combined with a thyroid cartilage reduction. It alters vocal quality to a more feminine pitch. It should only be attempted when speech therapy has failed, and usually requires follow-up speech therapy.

» Craniofacial surgery is a complex and sometimes very radical surgery that is sometimes helpful but should only be contemplated when treatment with hormones has been fully utilized and when simpler cosmesis has failed.

adjunct **augmentation mammoplasty**

Treatment recommended for SOME patients in selected patient group

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Ongoing

» Breast growth from cross-sex hormone therapy takes about 2 years and ultimately produces breasts that are typically one brassiere cup size smaller than in the patient's first-degree female relations.

» Although not a formal prerequisite, it is recommended that patients receive feminizing hormone treatment for a minimum of 12 months prior to augmentation mammoplasty.[1] In the author's experience, a minimum of 2 years is preferable. This is because it can be aesthetically problematic if natural breast development under estrogen stimulation follows an augmentation mammoplasty.

adjunct **genital surgery**

Treatment recommended for SOME patients in selected patient group

» Criteria for genital surgery include the following:[1] persistent, well-documented gender dysphoria; capacity to make a fully informed decision and to consent for treatment; relevant medical or mental health problems are well controlled; a minimum of 1 year of continuous hormone therapy and living in the desired gender role, unless hormone therapy is not medically indicated (many clinics would want 2 years). The patient must over that period of time have shown improved psychological, social, and, probably, occupational function.

» The surgery uses the existing genitals to fashion a vulva, neoclitoris and hood, labia, and (often) a neovagina. Preoperative genital hair removal is sometimes needed, particularly in patients who have been circumcised. The cosmetic results can be very good.

born females

born females **1st** **observation in changed sex role for ≥1 year**

» Treatment for gender dysphoria should not typically be started unless the patient has already changed gender role. This means legally changing registration to that of the preferred sex and changing the name on all documents. All other people should be made aware of this change and asked to treat the patient as this sex, even if they know this was not always the case.

» There is universal agreement within international standards of care that practical experience of at least 1 year (plus a year of continuous hormone treatment) should precede any genital surgery.[1] [27] Longer periods would

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Ongoing

be needed if there are any problems living in the new gender role. Patients should not undergo surgical treatment until they are thriving (not merely surviving) in their new gender role.

» Some patient groups maintain that hormone treatment should precede a change of gender role, but this approach involves a prolonged period of potentially dangerous treatment with hormones and may result in the patient being forever unhappy with the degree of bodily change and indefinitely postponing any change of role.

successful role change for ≥1 year **plus** **androgens**

Treatment recommended for ALL patients in selected patient group

» Criteria for hormone therapy include the following:[1] persistent, well-documented gender dysphoria; capacity to make a fully informed decision and to consent for treatment; relevant medical or mental health problems are well controlled.

» Contraindications to masculinizing treatment with testosterone include:[1] pregnancy; unstable coronary artery disease; untreated polycythemia with a hematocrit of 55% or higher.

» Most clinics require the patient to have already started living in the new gender role before this treatment is considered.

» Treatment is preferably done working as part of a multidisciplinary team containing (or having easy access to) an endocrinologist.

» Cross-sex hormone treatment aims to elicit in a born-female patient the secondary sexual changes seen in born males at puberty. These changes will be superimposed on whatever female pubertal changes have already occurred and will not reverse them.

» Androgens are administered in dosages sufficient to induce menopause, usually once monthly but, more rarely, as often as once every 2 weeks. Once menopause is achieved, it is often possible to decrease the frequency without menstrual periods returning.

» Gonadotropin suppression is generally not needed, as androgens alone usually suppress ovarian function very well.

» Preparations, doses, and licensing restrictions for testosterone vary according to country of practice. A variety of preparations and routes

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Ongoing

of administration are available, including injectables, gels, patches, and buccal tablets.

» The aim of therapy is to achieve serum testosterone levels in the normal physiological range for young males at all times. With topical testosterone preparations levels should be measured at least six hours after the preparation was applied, making sure the blood is drawn from a different site to the one the preparation was earlier applied. The level is constant and should be in the normal male range. Injected preparations need a peak and trough level. The trough is the level that pertains to the day the injection is due and should be at the bottom end of the normal male range. The peak level is that which applies a week after the injection is given, and should be at the top end of the normal male range. This ensures that at no point in the dosing cycle is the level supraphysiologically high or low. Longer acting preparations need a single, trough, measurement that should be at the bottom end of the normal range. Consult specialist for guidance on dose.

» Data from studies reported in the literature between 1980 and 2010 strongly suggest that treatment of female-to-male transsexuals with supra-physiologic doses of testosterone is associated with minimal adverse effects and no increase in mortality, breast cancer, vascular disease, or other major health problems.[31] However clinicians can achieve a good clinical response and minimize the risk of adverse effects by avoiding supraphysiologic levels of testosterone.

» It typically takes 2 or more years for patients to achieve maximal masculinizing results from hormones.[1]

» For patients who go on to have oophorectomy, hormone therapy with testosterone is usually continued lifelong, unless contraindications develop.[1]

adjunct **bilateral mastectomy**

Treatment recommended for SOME patients in selected patient group

» There is no consensus about when born-female patients should undergo bilateral mastectomy. Although hormone therapy is not a formal prerequisite to bilateral mastectomy,[1] most practitioners take the view that it should come after a change of gender role and treatment with androgens. Some patient groups would argue that it should precede both.

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Ongoing

adjunct **hysterectomy and bilateral oophorectomy**

Treatment recommended for SOME patients in selected patient group

» Consideration of hysterectomy and bilateral oophorectomy is recommended within 2 years to obviate the risk of gynecologic malignancy.

» Criteria for hysterectomy and bilateral oophorectomy include the following:[1] persistent, well-documented gender dysphoria; capacity to make a fully informed decision and to consent for treatment; relevant medical or mental health problems are well controlled; a minimum of one year of continuous hormone therapy and living in the desired gender role (unless hormone therapy is not medically indicated).

» The aim of hormone therapy prior to oophorectomy and hysterectomy is principally to introduce reversible estrogen suppression, before the patient undergoes irreversible surgical intervention.[1]

» For patients who have not had previous abdominal surgery, the laparoscopic technique for hysterectomy and bilateral oophorectomy is recommended to avoid a lower abdominal scar.[1]

» Other approaches are transvaginal and transabdominal. Vaginal access may be difficult as most patients are nulliparous and have often not experienced penetrative intercourse.[1] A transabdominal approach should utilize any incision other than a Pfannenstiel incision because this incision is pathognomonic of gynecologic surgery and the resulting scar looks odd in a male.

adjunct **phalloplasty**

Treatment recommended for SOME patients in selected patient group

» Criteria for phalloplasty include the following:[1] persistent, well-documented gender dysphoria; capacity to make a fully informed decision and to consent for treatment; relevant medical or mental health problems are well controlled; a minimum of 1 year of continuous hormone therapy and living in the desired gender role, unless hormone therapy is not medically indicated (many clinics would want 2 years). The patient must, over that period of time, have shown improved psychological, social, and, probably, occupational function.

» This is a complex, often multistage procedure.

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Ongoing

» Donor sites for phalloplasty can include the forearm, abdominal skin, or tissue from elsewhere on the patient's body. The complexity, duration, and expense of the procedure are such that only a large minority of patients chose to undergo this surgery.

» The cosmetic and functional results are fairly good, but the result, in even the best centers, is clearly distinguishable from a native penis.

adjunct **craniofacial surgery**

Treatment recommended for SOME patients in selected patient group

» This complex and sometimes very radical surgery is sometimes helpful but should only be contemplated when treatment with hormones has been fully utilized and when simpler cosmesis has failed.

Primary prevention

It is not clear whether it is desirable to attempt to prevent disorders of gender identity. Some people, particularly patient groups, would see this state as a natural variation in human expression and consider any attempt at prevention as being akin to eugenics. Primary prevention is, in any case, not currently possible.

Secondary prevention

Patients taking hormonal therapies should avoid prothrombogenic states such as obesity, smoking, or inactivity.

Patient discussions

Patients should be educated on the symptoms and signs of thromboembolic disease and advised to present promptly for investigation, should these symptoms occur.[1]

Patients receiving hormone treatment require information on the likely extent and timing of hormone-induced changes. Although the data on this is limited, and a large degree of natural variation can be expected, the following information from the Endocrine Society is helpful as a general guide.[27]

Expected timing of masculinizing effects of testosterone[27]

- Onset in the first 1 to 6 months:
  - Cessation of menses
  - Increased sexual desire
  - Increased facial and body hair (maximum effect 4-5 years)
  - Increased skin oiliness/acne (maximum effect 1-2 years)
  - Increased muscle mass (maximum effect 2-5 years)

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- Redistribution of fat to a more typically male pattern (maximum effect 2-5 years)
- Vaginal atrophy (maximum effect 1-2 years).

- Onset in the first year:
  - Deepening of voice (maximum effect 1-2 years)
  - Clitoromegaly (maximum effect 1-2 years)
  - Male pattern hair loss (some patients only).

Expected timing of feminizing effects of estrogen and antiandrogen therapy[27]

- Onset in the first 1 to 3 months:
  - Decreased sexual desire (maximum effect 3-6 months)
  - Decreases spontaneous erections (maximum effect 3-6 months).
- Onset in the first 3 to 6 months:
  - Redistribution of body fat to a more typically female pattern (maximum effect 2-3 years)
  - Decreased muscle mass and strength (maximum effect 1-2 years)
  - Softening of skin and decreased oiliness (maximum effect unknown)
  - Breast growth (maximum effect 2-3 years)
  - Decreased testicular volume (maximum effect 2-3 years).
- Onset in the first 6 to 12 months:
  - Decreased terminal hair growth (maximum effect greater than 3 years).
- Variable timing of onset:
  - Male sexual dysfunction
  - Decreased sperm production (maximum effect greater than 3 years)
  - Scalp hair.

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Monitoring

Monitoring

Clinical review

- For patients receiving hormone treatment, medical evaluation by the hormone-prescribing physician every 2 to 3 months in the first year, and every 6 to 12 months thereafter, is recommended.[1] [27] This is to monitor for appropriate signs of masculinization/feminization, and for the development of any adverse reactions (e.g., venous thromboembolism, cardiovascular impairment). It typically takes at least 2 years for patients to achieve maximal masculinizing/feminizing results from hormones.[1]
- Patients who undergo gonadectomy require hormone replacement treatment, surveillance, or both, to prevent adverse effects associated with chronic hormone deficiency.[27]

Blood tests

- For patients receiving hormone treatment, laboratory (blood test) monitoring is recommended every 2 to 3 months in the first year, and every 6 to 12 months thereafter. A clinical priority is maintaining testosterone/estrogen levels within the physiologic range for born-female/born-male patients respectively, given that supraphysiologic doses may lead to an increased risk of adverse effects.[27] Long-term monitoring of lipids, prolactin, LFTs (plus hematocrit in born females only) from baseline is advisable, although derangements are rare. The Endocrine Society guidelines contain detailed standard monitoring plans for patients on both testosterone and estrogen cross-hormone therapy, including recommended serum hormone levels.[27]

Mammography in born males

- It is not clear whether there is any need for mammographic breast cancer screening in born males. Data are sparse, but only 5 breast cancers have ever been reported in this patient group, and these were in patients on unsupervised treatment regimes that included progesterone (which raises the risk of cancer in born females on hormone replacement therapy). Avoiding the use of progesterone in treatment seems greatly to decrease the risk of breast cancer.[30] Based on a potential increased risk of breast cancer with feminizing hormones, the Endocrine Society guidelines suggest that born males taking feminizing hormones follow breast screening guidelines recommended for biological women.[27]

Mammography in born females

- If mastectomy has not been performed, standard breast screening guidance applies.

Prostate screening in born males

- Born-males treated with estrogens should follow screening guidelines for prostatic disease and prostate cancer recommended for biological men.[27]

Gynecologic monitoring

- Anyone with an intact uterus, cervix, or ovaries should be subject to the usual screens for malignancies of these organs, particularly because long-term androgen treatment is associated with endometrial hyperplasia. Total hysterectomy and oophorectomy should be considered, based on an evaluation of the risks and benefits.[27] Patients re-registered as male may be automatically dropped out of cervical cancer screening programs and need to remember to seek such screening without being reminded.

Bone mineral density measurement

- This is recommended for patients with risk factors for osteoporosis, and in particular for those who stop hormone treatment following gonadectomy.[27]

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Complications

Complications	Timeframe	Likelihood
estrogen- or androgen-related obesity	**long term**	**high**
Both estrogens and androgens increase appetite, so unless actual consumption is kept constant, weight gain will result.		
estrogen-related thromboembolic disease	**long term**	**low**
Estrogen treatment raises the risk of thromboembolic disease, particularly in smokers. Thromboembolic events are still not common and are usually not fatal. Because occlusive cardiovascular disease is rendered less common, all-cause mortality is not raised in treated patients.[37]		
androgen-related polycythemia	**long term**	**low**
Particularly before hysterectomy and oophorectomy, when higher doses of androgens may sometimes be employed to achieve menopause. Androgen treatment raises hematocrit, particularly in smokers. Hysterectomy and oophorectomy may allow dose reduction, or phlebotomy may be needed.[30]		
estrogen- or androgen-related hyperprolactinemia	**long term**	**low**
Particularly at outset of treatment. Estrogens and androgens can cause prolactin to rise. Only levels of over 1000 IU require endocrine advice.[30]		
estrogen- or androgen-related dyslipidemia	**long term**	**low**
Dyslipidemia is not common, but is worthwhile monitoring. If apparent it is treated in the usual manner with diet and statins.		
bone loss	**long term**	**low**
Bone mass is generally preserved with use of either sex steroid. The risk of osteoporosis is increased for patients who stop sex hormone treatment following gonadectomy.[27]		

Prognosis

Disorder of gender identity preceded by a gender dysphoria of childhood

Prognosis is generally very good, particularly for born-female patients. Most patients are lost to follow-up and go on to live ordinary lives in their new gender role. The technical success of surgery and a subsequent legal recognition of a change of sex relates strongly to good psychological and social outcome.[33]

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Disorder of gender identity preceded by a diagnosis of dual role transvestism

Prognosis is slightly more guarded. Regrets about gender reassignment surgery are associated with poor family and friend support, a lack of an earlier history of childhood gender dysphoria, and a lack of attraction to the same biological sex.[34] [35] In born-male patients, completed military service, a history of typically masculine, physically demanding jobs, and a comparatively late age (>30 years) at first request for surgery have been found to be negative prognostic factors in sex-reassignment evaluations.[36]

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Treatment guidelines

International

Endocrine treatment of gender-dysphoric/gender-incongruent persons (https://www.endocrine.org/guidelines-and-clinical-practice/clinical-practice-guidelines) [27]

Published by: Endocrine Society **Last published:** 2017

Guidelines for psychological practice with transgender and gender nonconforming people (https://www.apa.org/practice/guidelines) [32]

Published by: American Psychological Association **Last published:** 2015

Report of the American Psychiatric Association Task Force on treatment of gender identity disorder (https://www.psychiatry.org/psychiatrists/search-directories-databases/library-and-archive/resource-documents) [3]

Published by: American Psychiatric Association **Last published:** 2012

Standards of care for the health of transsexual, transgender, and gender nonconforming people (v7) (https://www.wpath.org/publications/soc) [1]

Published by: World Professional Association for Transgender Health **Last published:** 2011

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Online resources

1. WHO: International Classification of Diseases 11th Revision (https://icd.who.int/en) *(external link)*

2. APA: gender dysphoria (https://www.psychiatry.org/File%20Library/Psychiatrists/Practice/DSM/APA_DSM-5-Gender-Dysphoria.pdf) *(external link)*

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Key articles

- Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, v7. Int J Transgend. 2012;13(4):165-232. Full text (https://s3.amazonaws.com/amo_hub_content/Association140/files/Standards%20of%20Care%20V7%20-%202011%20WPATH%20(2)(1).pdf)
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Figure 1 – BMJ Best Practice Numeral Style

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